(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
18 November 2004 (18.11.2004)

PCT

(10) International Publication Number
WO 2004/099251 A3

(51) International Patent Classification[7]: C07K 16/14, A61K 39/395

(21) International Application Number: PCT/US2004/014276

(22) International Filing Date: 6 May 2004 (06.05.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/468,475	6 May 2003 (06.05.2003)	US
60/474,530	30 May 2003 (30.05.2003)	US
60/555,540	23 March 2004 (23.03.2004)	US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report: 28 April 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMPOSITIONS AND METHODS FOR TREATMENT OF CRYPTOCOCCOSIS

(57) Abstract: The invention described herein provides human antibodies produced in non human animals that specifically bind to *Cryptococcus neoformans* capsular glucuronoxylomannan (GXM). The invention further provides methods for making the antibodies in a non-human animal and for expressing the antibodies in cells including hybridomas and recombinant host cell systems. Kits and compositions comprising the antibodies are also provided in addition to methods of diagnosing, treating, inhibiting or preventing C. *neoformans* infection or conditions or disorders caused by such infection by administering to a patient the antibodies or compositions described herein.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/014276

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K16/14 A61K39/395

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, WPI Data, PAJ, EMBL

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MAITTA R W ET AL: "A conjugate of a Cryptococcus neoformans' GXM-mimotope generate different antibody responses in human immunoglobulin transgenic mice" ABSTRACTS OF THE GENERAL MEETING OF THE AMERICAN SOCIETY FOR MICROBIOLOGY, vol. 101, 2001, page 337, XP009039260 & 101ST GENERAL MEETING OF THE AMERICAN SOCIETY FOR MICROBIOLOGY; ORLANDO, FL, USA; MAY 20-24, 2001 ISSN: 1060-2011 abstract ----- -/--	1,3-8, 16-19, 24-43

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 November 2004	11. 03. 2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hermann, P

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INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PIROFSKI L ET AL: "Analysis of human monoclonal antibodies elicited by vaccination with a Cryptococcus neoformans glucuronoxylomannan capsular polysaccharide vaccine" INFECTION AND IMMUNITY, vol. 63, no. 8, 1995, pages 3005-3014, XP002303875 ISSN: 0019-9567 the whole document	1,3-8, 16-19, 24-43
P,X	MAITTA R W ET AL: "A monoclonal antibody from human immunoglobulin transgenic mice protects mice against Cryptococcus neoformans challenge." ABSTRACTS OF THE INTERSCIENCE CONFERENCE ON ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, vol. 43, 2003, page 435, XP001203719 & 43RD ANNUAL INTERSCIENCE CONFERENCE ON ANTIMICROBIAL AGENTS AND CHEMOTHERAPY; CHICAGO, IL, USA; SEPTEMBER 14-17, 2003 abstract	1,3-8, 16-19, 24-43
P,X	MAITTA ROBERT W ET AL: "Immunogenicity and efficacy of Cryptococcus neoformans capsular polysaccharide glucuronoxylomannan peptide mimotope-protein conjugates in human immunoglobulin transgenic mice." INFECTION AND IMMUNITY, vol. 72, no. 1, January 2004 (2004-01), pages 196-208, XP002303874 ISSN: 0019-9567 abstract	1,3-8, 16-19, 24-43
A	ZHONG ZHAOJING ET AL: "Antifungal activity of a human antiglucuronoxylomannan antibody" CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, vol. 5, no. 1, January 1998 (1998-01), pages 58-64, XP002303876 ISSN: 1071-412X the whole document	1,3-8, 16-19, 24-43
A	FLEURIDOR RICHARDSON ET AL: "A human IgM monoclonal antibody prolongs survival of mice with lethal cryptococcosis" JOURNAL OF INFECTIOUS DISEASES, vol. 178, no. 4, October 1998 (1998-10), pages 1213-1216, XP009039258 ISSN: 0022-1899 the whole document	1,3-8, 16-19, 24-43

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/014276

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 2, 9-11
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 35-40 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-11,24-43(all in part); 16-19(in full)

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-11, 24-43(all in part) and 16-19 (in full)

Invention 1 relates to a human monoclonal antibody or antigen-binding portion thereof; its variable light chain polypeptide and CDRs 1-3 characterized by SEQ. IDs. 5-8 respectively and nucleic acid sequences encoding said respective polypeptides characterized by SEQ. IDs. 17-20; its variable heavy chain polypeptide and CDRs 1-3 characterized by SEQ. IDs. 47-50 respectively and nucleic acid sequences encoding said respective polypeptides characterized by SEQ. IDs. 35-38 respectively; the cell line producing said antibody named G15B4G5 (ATCC PTYA-5171); a host cell transformed with said nucleic acid molecules; the method of producing said monoclonal antibody by culturing said transformed host cell; composition and kit comprising said antibody and method for the treatment of for the prevention of Cryptococcosis using said monoclonal antibody.

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2. claims: 1-11, 24-43 (all in part) and 12-15 (in full)

Invention 2 relates to a human monoclonal antibody or antigen-binding portion thereof; its variable light chain polypeptide and CDRs 1-3 characterized by SEQ. IDs. 1-4 respectively and nucleic acid sequences encoding said respective polypeptides characterized by SEQ. IDs. 13-16; its variable heavy chain polypeptide and CDRs 1-3 characterized by SEQ. ID. 43-46 respectively and nucleic acid sequences encoding said respective polypeptides characterized by SEQ. IDs. 31-34 respectively; the cell line producing said antibody named G14F7E5 (ATCC PTYA-5170); a host cell transformed with said nucleic acid molecules; the method of producing said monoclonal antibody by culturing said transformed host cell; composition and kit comprising said antibody and method for the treatment of for the prevention of Cryptococcosis using said monoclonal antibody.

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3. claims: 1-11, 24-43(all in part) and 20-23 (in full)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Invention 3 relates to a human monoclonal antibody or antigen-binding portion thereof; its variable light chain polypeptide and CDRs 1-3 characterized by SEQ. IDs. 9-12 respectively and nucleic acid sequences encoding said respective polypeptides characterized by SEQ. IDs. 21-24; its variable heavy chain polypeptide and CDRs 1-3 characterized by SEQ. IDs. 51-54 respectively and nucleic acid sequences encoding said respective polypeptides characterized by SEQ. IDs. 39-42 respectively; the cell line producing said antibody named G19B9G7 (ATCC PTYA-5172); a host cell transformed with said nucleic acid molecules; the method of producing said monoclonal antibody by culturing said transformed host cell; composition and kit comprising said antibody and method for the treatment of for the prevention of Cryptococcosis using said monoclonal antibody.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/014276

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 075 181 A (KUCHERLAPATI RAJU ET AL) 13 June 2000 (2000-06-13) the whole document	1,3-8, 16-19, 24-43
A	WO 01/25492 A (BIOSITE DIAGNOSTICS INC ; GRAY JEFF (US); BUECHLER JOE (US); LONBERG N) 12 April 2001 (2001-04-12) the whole document	1,3-8, 16-19, 24-43

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US2004/014276

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